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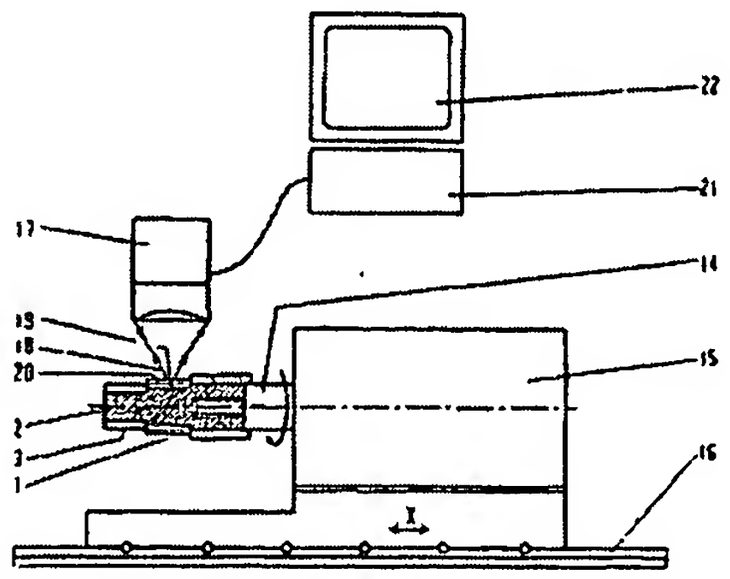
DE-Z.: GREULICH, K.O.: *Lasermikrosonden*[1] *und Laserspektroskopie*[2], in: *Physik in unserer Zeit*, no. 4, p. 170-175

[54] Process for the Microscopic Investigation of the Tissue Integration of Solid Bodies[3], which are Permanently or Temporarily Implanted into Living Organisms, and Device for the Performance of the Process

[57] With the process for the microscopic investigation of the tissue integration of solid bodies, which are permanently or temporarily implanted into living organisms, and the device for performing the process it is provided that the preparation[4] (**1**), consisting of a solid body and the overlaid tissue layer (**3**), is subjected to pretreatments for the stabilization and hardening of the tissue layer (**3**), which are followed by abrasion processes. The preparation (**1**) is then moved along by means of a measurement adapter (**14**) of a handling system (**15**) in front of the recording optics of a microscope. The set plane of investigation (**20**) is thereby scanned by the microscope and the microscopic images obtained in this way are transformed by means of an appropriate video camera into electrical signals which are stored by means of an EDP[5] [unit] (**21**) and, in conjunction with the video signals which were obtained from the scanning of other planes of investigation (**20**), assembled into a three-dimensional image. The other planes of investigation (**20**) are obtained via abrasion processes on the preparation (**1**), or by adjusting the focusing on the microscope.



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[1] typographic error in the original
[2] *Laser Micro-Probes and Laser Spectroscopy*
[3] or *objects*
[4] or *specimen*
[5] *Electronic Data Processing*

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Description

The process for the microscopic investigation of the tissue integration for solid bodies which are permanently or temporarily implanted into living organisms, and the device for performing the process serve in the exploration of implants and other solid bodies which are inserted into the living tissue and are supposed to intergrow or not intergrow with the tissue. A special research focus in this context exists in dental medicine.

In addition to the usual dental treatment and the utilization of prostheses, the considerable advances in dental medicine of the past years makes it possible also for implants to be inserted directly into the jaw bone. Today, this new method of treatment has indeed already found broad application, there is nevertheless now as ever a certain need for research, in particular in conjunction with the intergrowing of the implants with the bone tissue.

One can only speak of a successful operation with long term success if the implant is perfectly osseointegrated (grown onto [the bone]). But also with other treatments are implants of various kinds introduced into the tissue.

The present invention proposes a method of investigation by means of which the osseointegration can be examined over the entire contact surface between implant and jaw bone. This is of great significance in conjunction with the development of the implant and their surface treatment. The proposed method of investigation can be used also in conjunction with other solid bodies which are permanently or temporarily introduced into the tissue. With such solid bodies one may deal with any implants which are to intergrow with the tissue, but also with surgical aids which after some time are removed again, e.g., when fractures are healed and for which an intergrowing is not desired.

In order to simplify the language, the process according to the invention is described in the following text in conjunction with implants. The course of action described there, however, is equally so in force for any other kind of solid bodies which are introduced into the tissue.

The following three publications are to be appreciated in conjunction with prior art:

1. The publication by GREULICH, K.O.: *Lasermikrosonden und Laserspektroskopie*[6]; in: *Physik in unser Zeit*, 1993, no. 4, p. 170-175 became known in conjunction with the investigation of biological preparations. Here, though, it is described how ultra-fine cell components can be mechanically moved under the microscope by means of the IR laser and cutting and other subdivision processes can be performed by means of the UV laser.

Not described is the tissue integration on implants. In this respect the patent application is not anticipated by this publication.

2. Described in the European patent EP 0 162 681 A2 is a microscopic method of investigation for which the radiation behavior of surfaces is investigated when being heated by means of lasers. The surfaces to be examined are moved back and forth in X and Y direction in front of the experimental setup and the reflection behavior is determined with a second laser beam.

The generation of three-dimensional images in conjunction with organic preparations is not provided. The invention here[7] is thus not affected by this patent.

3. A milling[8] machine is described in the German patent DE 31 13 718 C2. Investigative procedures for biological preparations are not subject matter of this patent. It does thus not preclude the invention here.

Disadvantages as follows result when exploring the osseointegration by means of methods according to the state of the art:

In order to introduce the implant one produces at first an appropriate borehole in the jaw bone, into which one then inserts the implant. With this one usually deals with a rotationally symmetric metal body, e.g., of titanium or a titanium alloy, the surface of which can be structured by mechanical processing, where threads are also possible. The healing of the implant in the bone is promoted through [the] anodic oxidation of the implant surface in an electrolytic bath and the utilization of materials which promote the osseointegration.

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[6] *Laser Microprobes and Laser Spectroscopy*
[7] literally: *own invention*
[8] or *grinding*

For the further course of the invention, the implant is placed in the bone in correct positional arrangement and the opening sutured shut so that the approx. four months healing phase can proceed undisturbed. The mucosa is then opened again and after a few intermediate steps, which serve in particular the reconstruction of the soft tissue, the so-called build-up is fastened to the implant by means of screws. Placed onto the build-up is then the crown, which forms the visible dental replacement.

With the research work in conjunction with the osseointegration of dental implants that became known until now, the relevant part of the jaw bone with the implant is extracted (e.g., animal experiment) and longitudinal sections were prepared. But only 2-3 preparations per implant can be examined with this method, which is linked to the thickness of the tools and other factors. In view of the very high overall expenditure, this is extremely disadvantageous as the gain of knowledge is only small. Of disadvantage are also the changes on the preparations which are caused through the sawing.

The object of the present invention is to create three-dimensional images of the entire tissue structures in the vicinity of the implant surfaces, so that the degree of tissue integration may be evaluated. The means for attaining this object are in the characteristics of the patent claims 1 and 20.

With the process according to the invention for the microscopic investigation of the tissue integration of solid bodies, which are permanently or temporarily implanted into living organisms, and the device for performing the process, the disadvantages mentioned are avoided as follows:

I. The preparation extracted from the jaw, consisting of implant and surrounding tissue (bone and soft tissue) is pretreated, e.g., embedded in paraffin or synthetic material or deep frozen. By that, the tissue is stabilized (conserved) biologically and hardened so far that a mechanical processing becomes possible, with a removal in layers of individual tissue layers.

II. The preparation pretreated in agreement with Point I is processed on an ablation device, e.g., the milling machine according to the invention, such that the rotationally symmetric implant is still enclosed only in a thin tissue layer, the thickness of which is, e.g., 100 µm or less.

Following the abrasive process, the surface of the layer of tissue thereby consists preferably of material which is not influenced by the osseointegration, so that no information is lost. But the investigation may also be started in deeper-lying layers. In this case one then abrades more material accordingly. But one can also abrade preparations, the implants of which have planar surfaces. The milling machine is then designed appropriately.

For the ablation of the tissue one may also use cutting processes like turning or milling. This is valid in particular if at first only a very rough material ablation is to take place. The modern laser technology offers another possibility for the removal in layers of the tissue on the implant. Also for reasons of simplifying the language, only the work with the milling machine according to the invention is described more closely in the text that follows. The facts of the case are, though, valid also for other ablation methods.

III. The tissue layer is then examined by means of a scanning microscope which works with a confocal laser, with respect to the osseointegration over the entire periphery (circular viewing), where by means of this microscope it is possible to make visible also the deeper-lying tissue layers in preset planes. By means of EDP one can create from this a three-dimensional image of the tissue structure which includes the entire circumference of the implant. Planar surfaces may also be investigated, which however will not be looked at more closely.

For the examination of the preparations one may also use other devices, e.g., fluorescence microscopes. Based on the particular advantages of the scanning microscopes with [a] confocal laser and also for simplifying the language, only the latter named microscope is mentioned in the text that follows. The presented facts of the case are, though, valid for other microscopes.

IV. If needed, the abrasion process corresponding to Point II, and the investigation according to Point III can be repeated so that the thickness of the tissue layer is in the end so thin that also the surface of the implant can be made visible with the scanning microscope.

The EDP [unit] then compiles the images, which were recorded following the abrasion processes, into a three-dimensional overall image which reproduces the

total interfacial area at the circumference of the implant. This overall image can be viewed in any planes and views.

With the process according to the invention and the device for performing the process one can thereby investigate the entire tissue which is involved in the osseointegration of the implant. During the investigation, no tissue material is lost which has not been examined microscopically beforehand, where the results are stored electronically. By means of EDP it is furthermore possible to represent the osseointegration in three dimensions.

The process according to the invention for the microscopic investigation of the tissue integration of solid bodies which are permanently or temporarily implanted into living organisms and the device for performing the process are described in detail in the following:

Regarding Point I

The implant with the part of the tissue (bone and soft tissue) surrounding it is extracted from the jaw and this preparation is at first pretreated for the further processing, e.g., embedded or subjected to a freeze treatment. Suitable for this are the processes introduced in histology.

1. Paraffin Method

The water is withdrawn from the preparation in a plurality of steps through treatment with alcohol and then removed through treatment with xylene which removes alcohol. A soaking may then take place in fluid paraffin, which is soluble in paraffin.

To accelerate the penetration one may also use a pressure swing adsorption with vacuum. Following the embedding process and the solidification of the paraffin, the preparation can be processed mechanically, which is also valid for the soft tissue present on it.

2. Resin Method

The preparation is similar to the paraffin method, i.e., the removal of water takes place first, which is followed by the resin infiltration, for which one usually uses photocuring acrylic resins. With this kind of embedding one can produce particularly strong, i.e., mechanically stable preparations.

3. Cryogenic Method

In this case, the preparation is cooled very fast to low temperatures and the examination is performed without the refrigerating chain being thereby allowed to be interrupted. Of advantage thereby is that the preparation experiences no changes as is the case with the embedding processes corresponding to Point 1 and 2, it is, though, not very easy to maintain the low temperatures in all stems of the method.

In the following, the embedded or deep frozen preparations are referred to only as preparations, without reference to the respective pretreatment.

Regarding Point II

The preparations are at first prepared coarsely on a milling machine according to the invention and then abraded again in the fine range. The milling machine has for this [reason] a power-driven tool spindle, which is fastened to the machine frame and holds a grinding disk of suitable dimensions, which may consist of corundum or another suitable material.

The preparations are fastened in the holding device of a work piece spindle, also power-driven, the geometric axis of which runs parallel to that of the tool spindle. The work piece spindle is connected to a Y-carriage, which allows for movement perpendicularly to its axis.

The Y-carriage is in turn connected to an X-carriage, which makes movement possible in the direction of the work piece spindle. In addition to this, the work piece spindle can be rotated with respect to the Y-carriage, around an axis C which is perpendicular to the direction of movement of the Y-carriage. The guiding and driving of the X-carriage and the Y-carriage as well as of the C-axis are performed at great precision so that feed movements in the µm range are possible during grinding.

It is provided for the machine to be equipped with CNC control, by means of which the entire process can be operated and controlled after the geometry of the implant and the desired layer thickness of the remaining tissue have been entered.

The distance between the cutting edge of the grinding disk and the axis of the tool spindle is determined by means of a device, which is fastened for this purpose to the spindle, similarly to the preparation.

The inside thread, which is anyway present on the implant, can advantageously be used for fastening the preparation to the holding device of the work piece spindle. But other possibilities for fastening are also provided. The grinding process is then performed under addition of cooling fluid. If one works with the cryogenic method one must cool the cooling fluid at least to the temperature of the preparation. One may consider for this application, e.g., alcohols. In conjunction with the cryogenic method, the cooling fluid has the additional function of keeping the temperature of the preparation low, one may possibly have to cool the holding device of the work piece spindle, too. In any case, it must be produced from an insulating material.

The cooling fluid can also be used for the cooling of the holding device, where it can be supplied to it via a rotary feed-through. Pelletier elements, though, are also provided, which are provided with electrical energy via slip rings or else also other cooling devices.

During the grinding process, the two spindles rotate in opposite directions, where the feed movements depend on the shape of the implant:

- With a cylindrically shaped implant one positions at first, with the spindles running, the free end of the implant with respect to the grinding disk through movement in the X direction, and then one brings the grinding disk and the preparation into contact through movement in the Y direction. One then removes the first layer of material through the controlled movement in the C direction over the length of the preparation. Following this is a second feed movement in the Y direction and removal of material through movement in the X direction, and so forth, until the desired small layer thickness of tissue material on the implant is reached.
- In case of stepped implants, for which the outside diameter, seen in longitudinal direction, becomes stepwise smaller, each step is processed separately, whereby

one starts with the large diameter. At first one performs a feed movement in Y direction, until the desired removal of material takes place, and then the preparation is moved in X direction until it is processed over its entire length. Then a new feed movement in the Y direction and a movement in X direction take place.

When the desired, very small layer thickness of the tissue material is then reached in the area of the large outside diameter, the preparation is moved in X direction so far until the grinding disk can be used with the next step of the outside diameter. The sequence of operation is then as described beforehand.

This is valid also for the further steps of the implant. As a result of the work, the stepped implant is finally covered over its entire outer periphery with a uniformly thin layer of tissue.

- The sequence of operations with a spherical implant is similar as with a cylindrically shaped implant. In this case, however, the work piece spindle is rotated around the C axis until the distance between the surface of the implant and the grinding disk remains constant when moving the X carriage. The desired, thin layer thickness of tissue material on the implant is achieved through feed movement in Y direction and removal of material through movement in Z direction.

In principle it is also possible to process preparations in which the implants have planar surfaces. To abrade the tissue layers, the grinding machine according to the invention is then designed as [a] surface grinding machine. The processing possibility, though, is not described more closely.

Regarding Point III

After the preparation has been abraded as described in Point II, to where the desired layer thickness of the tissue is present on the implant, one can commence with the circular viewing. According to the invention one uses a scanning microscope for this, which operates with a confocal laser through which it is possible to capture not only the surface of the preparation, but also to investigate deeper [lying] tissue layers at a

precisely given depth. The defined plane of investigation is scanned point for point by the scanning microscope and the digitized results are stored by means of EDP.

The sequence of operations is then as follows: The abraded preparations is fastened by means of the implant thread, [in a] twist-proof [way], to the adapter of a handling system. With the implant as well as the adapter on can make arrangements which allow for the same angular position (twist angle) to always be achieved with great accuracy between the implant and adapter even under repeated removal and renewed fastening of the preparation.

Attention is paid to a good repeatability of the coordinates also with respect to the axial fastening of the preparation to the adapter. The handling system has a device by means of which the preparation can be rotated around its longitudinal axis and shifted parallel to this axis (X direction). Measurement devices are furthermore present, which allow for the angle of rotation as well as the linear movement in the X direction to be captured very accurately. During the examination, the preparation is shifted with the handling system in X direction in front of the optical elements of the microscope and, following the scanning of one envelope line, rotated by one angular step. The longitudinal axis of the preparation is thereby oriented so that the distance between the optical elements of the microscope remains constant during the longitudinal shifting, and the focus of the optical path remains in the intended plane of investigation.

The scanning microscope is at first adjusted onto the surface of the preparation as the first plane of investigation and the vertical line is scanned point for point The preparations is then rotated by a small angular step and the new vertical line is also scanned point for point. The spacing of the scanned points and the envelope lines (vertical lines) may be varied. The smaller this spacing is, the large is the resolution of the generated images. After the entire circumference has finally been scanned, following the rotation of the preparation by 360°, the microscope is adjusted to a second plane of investigation which lies by a certain extent under the surface of the preparation and also has the shape of a cylinder envelope. The process of measuring is then repeated point for point as described before.

Following the scanning of this second plane of investigation one may adjust to and scan additional planes of investigation. All results are stored in an EDP [unit] and

transformed there into three-dimensional images, where each of the phase angles and the coordinates in X direction are assigned. For the evaluation, images can be accessed in any cross-sectional or longitudinal section, also with the indication of the position in the preparation.

But images are also possible from any other section plane. Through that one can represent the osseointegration of the implant over the entire extent. In principle it is also possible to examine preparations with the scanning microscope, the implants of which have planar surfaces. The handling system in this case is configured such that the preparation can be moved linearly along two axes at a right angle to one another. However, this possibility is not described any further in the following.

Regarding Point IV

Should one want to investigate on the preparation tissue layers which are thicker than what the penetration depth of the microscope allows, following the first recording according to point III one can repeat the grinding process according to point II.

Somewhat less material is grinded off than what corresponds to the penetration depth of the microscope.

The newly formed surface then still belongs to the tissue layer which was recorded at the first recording. Following this mechanical processing one proceeds as is already described under point III, i.e., starting out at the surface of the preparation one scans point for point one plane of investigation after another and the values are stored, where all planes of investigation have the shape of cylinder envelopes of various diameters. This process of grinding and investigation can be repeated multiple times.

In the end, the objective is to extend the microscopic investigations down to the surface of the implant. With this multiple investigation it is particularly important that for every new measurement process, the preparation is fastened to the measurement adapter in a positionally controlled [manner].

The data can then be compiled by means of the EDP [unit] and suitable software from all the investigation planes into a three-dimensional overall image. When individual planes of investigation were scanned repeatedly with the microscope, e.g., as the lower plane following the first grinding and the upper layer following the second grinding, the

surplus data are recognized and deleted, so that the overall image is not interrupted by doublings. In order to recognize the surplus data one can compare with one another the digitized image data, as well as the geometric data. The advantage of the EDP [unit] consists further on in that, following the availability of the three-dimensional image information, any section images can be retrieved, also with respect to their position in the preparation. With that it is possible to precisely evaluate the osseointegration in any position.

In the following, the process according to the invention for the microscopic investigation of the tissue integration of solid bodies, which are permanently or temporarily implanted into living organisms, and the device for performing the process are explained more closely on an example and by means of the **Fig. 1** through **4**. Other embodiments are also considered. The images show in this respect examples of embodiment of a plurality of other conceivable [embodiments].

Fig. 1 shows the processing device according to the invention designed as grinding machine. In the case of the solid body one deals with a stepped implant.

Fig. 2 shows the actual measurement set-up consisting of a handling system, a scanning microscope with digital video camera and an EDP [unit]. The preparation to be investigated is mounted on the handling system.

Fig. 3 shows the scanning with the scanning microscope of the first tissue layer of the preparation.

Fig. 4 shows the scanning of the tissue layer of the preparation following the grinding removal of the first layer of tissue.

Regarding **Fig. 1**

The figure shows a top view of the grinding machine in the idle position. But other setups of the individual machine components are possible. The machine can be equipped with a CNC control.

The preparation (**1**), consisting of the implant (**2**) with the tissue layer (**3**), which had already been preground roughly, is fastened by means of an adapter (**4**) to the work piece spindle (**5**), which can be power-driven by a motor.

The work piece spindle (**5**) is rotatable in a certain angular range around the C axis (**6**) and connected to the Y-carriage, which is held by guides (**8**) which make possible translatory movement in the Y direction. The guides (**8**) are fastened to an X-carriage (**9**), which is held by guides (**10**) which are connected to the machine frame (**11**). The movements about the C axis (**6**) and/or in the X and Y direction can be performed manually or else also by machine power. The latter is valid in particular with CNC control.

Also fastened to the machine frame (**11**) is the toll spindle (**12**), which at its front end holds the replaceable grinding disk (**13**) and also has a power drive. The contact with the grinding disk (13) can be established through movement of the preparation (**1**) via the Y-carriage (**7**) and the X-carriage (**9**) and the grinding process may proceed.

The implant (**2**) and the grinding disk (**13**) thereby rotate in opposite directions. At the onset of the grinding process, a feed movement by the desired extent is performed in the Y direction and then the desired material removal is undertaken via the grinding process, through feed movement in the X direction.

Regarding **Fig. 2**

Represented in this Figure is the actual measurement procedure by means of [the] scanning microscope (**17**) which is equipped with a confocal laser. The preparation (**1**), consisting of [the] implant (**2**) and tissue layer (**3**), is fastened to the measurement adapter (**14**) of the handling system (**15**) and can be moved by this rotationally as well as translationally in the indicated X direction. Appropriate drive motors (not drawn) are provided for moth movements. The handling system (**15**) has a linear guide (**16**) and measurement devices for capturing the longitudinal displacement in the X direction and the twist angle. The corresponding geometric data are digitized and fed to the EDP (**21**) [unit].

The scanning microscope (**17**) in the representation is adjusted so that the optical path (**18**) is adjusted onto about the center of the layer of tissue (**3**), see in radial direction, and records the measurement point (**19**) which lies in the plane of investigation (**20**), which has the shape of cylinder envelope and is represented in the sectional drawing as a line. Through movement of the handling system (**15**) with the

preparation (1) in the X direction one can record point for point all measurements in the vertical line of the plane of investigation (20).

When all points of the first vertical line have been recorded, then the measurement adapter (14) with the preparation (1) performs a rotation by a small angular step and another envelope line within the plane of investigation (20) becomes the vertical line and can also be scanned point for point, again through movement in the X direction. this process is repeated until the entire surface of the plane of investigation (20) has been scanned.

The scanning microscope (17) is then newly adjusted to another plane of investigation, which also represents a cylinder envelope, though with a smaller radius. The scanning process is the repeated as previously described.

One plane of investigation after another are scanned as described, until the tissue layer (3) has been investigated to the extent that is possible with the scanning microscope (17), in agreement with the penetration depth of the confocal laser. If the preparation (1) is to be investigated at even greater depth, then it is taken off the measurement adapter (14) and the tissue layer (3) is further removed through abrasion, so that one may reach also deeper lying investigation layers. The preparation (1) is then fastened again in a positionally controlled [manner] to the measurement adapter (14) and the investigation is repeated. The entire process, grinding and investigation, can be repeated until the surface of the implant can also be made visible.

Connected to the scanning microscope (17) is an EDP (21) [unit] which collects all data, including the geometrical data of the measurement systems. The digitized data supplied from the scanning microscope are compiled into a three-dimensional image. This can be made visible on a screen (22) in any desired section, but the usual printouts in color are also possible. The geometric data for any image of a section may also be made visible. In order to improve the contrast or to make special structures or effects visible it is possible to place various filters in to the optical path of the scanning microscope (17).

Regarding **Fig. 3**

In this Figure it is shown once more how the optical path (**18**) of the scanning microscope (**17**) is focused onto one measurement point (**19**) in a relatively far outside lying plane of investigation (**20**) of the layer of tissue (**3**) of the preparation (**1**)

The thickness of the tissue layer (**3**) was removed such that it can be scanned with the scanning microscope (**17**) down to its midpoint. After the appropriate measurement program has been performed, then the preparation (**1**) is taken from the measurement adapter (**14**) of the handling system (**15**) and the layer of tissue (**3**) is reduced to one half of the thickness.

Regarding **Fig. 4**

This Figure shows the same preparation (**1**) as represented in **Fig. 3**, however, with the layer thickness reduced to one half of the tissue following 2nd grinding process. The optical path (**18**)of the scanning microscope (**17**) is focused onto a measurement point (**19**) which lies in a central plane of investigation (**20**) of the remaining tissue layer (**3**). The scanning process runs again as already described several times.

List of Reference Numbers

1 Preparation
2 Implant
3 Layer of tissue
4 Adapter
5 Work piece spindle
6 C axis
7 Y carriage
8 Guides
9 X carriage
10 Guides
11 Machine frame
12 Tool spindle
13 Grinding disk
14 Measurement adapter
15 Handling system
16 Linear guide
17 Scanning microscope
18 Optical path

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19 Measurement point
20 Plane of investigation
21 EDP [unit]
22 Screen

Patent Claims

1. Process for the microscopic investigation of the tissue integration for solid bodies which are permanently or temporarily implanted into living organisms, **characterized in** that the corresponding preparation (**1**), consisting of a solid body and the overlaid tissue layer (**3**), is subjected to pretreatments for the biological stabilization and hardening of the tissue layer (**3**), which are followed by abrasion processes in which the tissue layer (**3**) is ablated to the desired thickness (**3**) and the preparation (**1**) is then fastened to the measurement adapter (**14**) of a handling system (**15**) and then moved by this along given paths in front of the recording optics of a microscope, where the adjusted plane of investigation (**20**) is scanned by the microscope point for point and the thus obtained microscopic images are either observed and/or photographed, or converted into electrical signals by an appropriate video camera, where said signals are stored by means of an EDP (**21**) [unit] and, together with the video signals which were acquired while scanning other planes of investigation (**20**), compiled into a three-dimensional image , where the other planes of investigation (**20**) are obtained via ablation processes on the preparation (**1**) or through adjustment of the focusing on the microscope.

2. Process according to claim 1, characterized in that, for the pretreatment, the preparation (**1**) is dehydrated and soaked with paraffin.

3. Process according to claim 1, characterized in that, for the pretreatment, the preparation (**1**) is dehydrated and soaked with synthetic resin.

4. Process according to claim 1, characterized in that, for the pretreatment, the preparation (**1**) is deep-frozen.

5. Process according to claim 1 through 4, characterized in that a scanning microscope (**17**) with confocal laser is used as microscope.

6. Process according to claim 1 through 5, characterized in that the preparation (**1**) rotates during the grinding process or other ablation processes.

7. Process according to claim 1 through 6, characterized in that during the grinding process or other ablation processes, the preparation is irrigated with a cooling fluid, which may also be deep frozen.

8. Process according to claim 1 through 7, characterized in that a grinding device or a turning, milling or laser processing machine is used, which has devices which allow for the preparation (1) to be processed such that afterwards the tissue layer (3) has a uniform layer thickness over the entire surface of an implant of any shape.

9. Process according to claim 1 through 8, characterized in that a grinding device or another ablation device is used, the entire sequence of motions is controlled and operated by a CNC control, into which one may also enter the geometric data of the implant (2) as well as the desired layer thickness of the tissue.

10. Process according to claim 1 through 9, characterized in that a scanning microscope (17) with confocal laser is used for the investigation of the ablated preparation (1), which [microscope] forms with the handling system (15) a rigid entity and transmits digitized image and geometry data to an EDP (21) [unit].

11. Process according to claim 1 through 10, characterized in that a handling system (15) is used, by means of which the preparation (1) can be moved translationally along two axis perpendicular to one another, where the spacing between the plane of investigation (20) and the optics of the scanning microscope (17) can be kept constant through movement along these axes.

13. Process according to claim 1 through 12, characterized in that a handling system (15) is used which has measurement systems by means of which its rotational and/or translatory movements can be captured and transformed into digital signals, which are stored by means of the EDP (21) [unit], together with the image data of the video camera of the scanning microscope (17).

14. Process according to claim 1 through 13, characterized in that, during the investigation, filters can be switched into the optical path of the scanning microscope (17).

15. Process according to claim 1 through 14, characterized in that, following the first investigation with the scanning microscope (17), at least one further ablation process is performed on the preparation (1), and at least one further investigation follows.

16. Process according to claim 1 through 15, characterized in that the geometric measurement data with respect to the rotational and/or translatory movements, which are recorded by the measurement systems of the handling system (**15**) and converted into digital signals, are coordinated by the EDP (**21**) [unit] with the image data of the scanning microscope (**17**).

17. Process according to claim 1 through 16, characterized in that the EDP (**21**) [unit] is equipped with software which allows to compile image data from several measurement procedures, between which there may lie ablation processes, such that one consistent, three-dimensional image forms and data which are present due to overlapping are being deleted, where oné performs for this either a comparison of the image data or of the geometric measurement data.

18. Process according to claim 1 through 17, characterized in that the three-dimensional images of the preparation (**1**) generated and stored in the EDP (**21**) [unit] can be made visible on the screen (**22**) as any section or printed, even in color, with a printer, preferably a sublimation printer.

19. Process according to claim 1 through 18, characterized in that the section images of the preparation (**1**) can be made visible or printed together with the geometric measurement data of the handling system (**15**).

20. Device for the microscopic investigation of the tissue integration of solid bodies, which are permanently or temporarily implanted into living organisms,, characterized in that processing device is present, which has adapters for holing the preparation (**1**) and tools for the ablation in layers of a tissue layer (**3**),

that a handling system (**15**) is present, which has a measurement adapter (**14**), which is connected to linear guides (**16**) and has measurement systems by means of which rotational and/or translatory movements can be captured and transformed into digital signals,

that a microscope is present for the investigation of the tissue layer (**3**), which is connected to the handling system,

that a video camera is present, which is connected optically to the microscope and electrically to an EDP (**21**) [unit] which has a software by means of which the images of various planes of investigation (**20**) can be compiled into one three-dimensional image.

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21. Device according to claim 20, characterized in that the processing device is designed as grinding machine which has an electrically driven tool spindle (**12**), which is connected to a machine frame (**11**) and holds the grinding disk, and an electrically driven work piece spindle (**5**) is further present, to the adapter (**4**) of which the implant (**2**) is fastened and which is connected via a C axis (**6**) to a Y carriage (**7**), which has guides (**8**), where the guides (**8**) are fastened to an X carriage (**9**), which has guides (**10**).

22. Device according to claim 20 through 21, characterized in that the grinding machine is equipped with a CNC control.

23. Device according to claim 20 through 22, characterized in that the grinding machine is connected to a cooling device, by means of which the cooling fluid for the cooling of the preparation (**1**) is cooled to temperatures below zero [°C].

24. Device according to claim 20 through 23, characterized in that the adapter (**4**) has a cooling device and/or a thermal insulation is present with respect to the tool spindle (**5**).

25. Device according to claim 20 through 24, characterized in that devices are present which allow for the same cooling fluid, which is provided for the cooling of the preparation (**1**), to be used also for the cooling of the adapter (**4**).

26. Device according to claim 20 through 25, characterized in that devices are present on the measurement adapter (**14**) of the handling system (**15**) as well as on the implant (**2**) which allow for the preparation (**1**) to be fastened to the measurement adapter (**14**) in a positionally controlled manner.

27. Device according to claim 20 through 26, characterized in that a linear guide (**16**) for the X direction, which is connected to an electric [power-]drive, is present on the handling system (**15**).

28. Device according to claim 20 through 26, characterized in that two linear guides, which are preferably arranged perpendicularly to one another, are present on the handling system (**15**).

29. Device according to claim 20 through 28, characterized in that the measurement adapter (**14**) has an electrical [power-]drive for continuous rotation or rotational movements in angular steps.

30. Device according to claim 20 through 29, characterized in that the measurement adapter (**14**) of the handling system (**15**) is connected to a cooling device and/or thermally insulated with respect to the handling system (**15**).

31. Device according to claim 20 through 30, characterized in that a scanning microscope (**17**) with [a] confocal laser is available as microscope.

32. Device according to claim 20 through 31, characterized in that for the visualization of the results, the EDP (**21**) is connected to at least one screen (**21**) and printer.

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